DETAILED ACTION

Acknowledgement of Receipt

Applicant's Response, filed 3/24/2011, in reply to the Office Action mailed 12/7/2010, is acknowledged and has been entered. Claims 1 and 5-8 are pending, of which claims 5-8 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claim 1 is readable upon the elected invention and are examined herein on the merits for patentability.

Response to Arguments

Any rejection not reiterated herein has been withdrawn as being overcome by amendment.

Applicant's arguments have been fully considered, but are not persuasive for reasons set forth hereinbelow.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pugsley *et al.* (*J. Cardiovascular Pharmacology*, 1998, 32(6), p. 863-874) and Gehrmann *et al.* (J. Cardiovascular Electrophysiology, 2000, 11(3), p. 354-368), in view of Knobloch (*Naunyn-Schmiedeberg's Arch Pharmacol.*, 2002, 366, p. 482-487), in further view of Rotolo (US 5,445,149), for reasons set forth in the previous Office Action.

Applicant argues on pages 4-5 of the Rejection that the Examiner concluded that it would have been obvious to one of ordinary skill in the art, from the teachings of Pugsley et al., Gehrmann et al., and Knoblich et al. to determine an in vivo cardiac electrophysiology profile of a compound affecting a cardiac ion channel, such as potassium channel, including Kv1.5, in rat, upon administration of the compound and simultaneous measurement of atrial refractory period and electrocardiograph interval, but points out that one could not determine the cardiac electrophysiology profile of the calcium channel blocker amlodipine, a compound which affects a cardiac ion channel, using the claimed method. Applicant asserts that while the Examiner stated it would be obvious to use the claimed method to determine the electrophysiology profile of a compound affecting a cardiac ion channel, however Applicants have found that the

method is useful for compounds affecting the Kv1.5 potassium channel, but not compounds such as those affecting the calcium ion channel.

This is not found to be persuasive. As set forth in the Specification in Example 3 and in paragraph 4 of the Response filed 3/24/2010, Applicant notes that while no change in heart rate and no change in AV nodal conduction or refractoriness was observed for amlodipine, diltiazem resulted in significant decrease in heart rate and significant increases in AV nodal conduction and refractoriness. Therefore, the claimed method has success with at least some calcium ion channel antagonist compounds (e.g. at least diltiazem). In addition, the rejection addresses the Kv1.5 ion channel specifically (see pages 9-11 of previous Office Action), as required by the limitation of instant claim 1.

Applicant further argues on page 10 of the Response that the claimed procedure differs from Pugsley to provide significant off target activity information. Applicant asserts that Pugsley et al. do not administer recording and stimulating catheters into the right jugular vein and common carotid artery of the rat. Applicant argues that Puglsey in combination with Gehrmann, Knobloch and in further view of Rotolo do not make the claimed invention obvious. Applicant argues that Gehrmann et al. describes electrophysiology studies in genetically engineered mice. In the epicardial study, wires are placed on the right ventrical, left ventrical and right atrium. In the intracardial study, a catheter is advanced from the right internal jugular vein through the right atrium to the right ventrical. Knobloch teaches a study of selective human cardiac ultrarapid delayed rectifier potassium current blockers in pigs. Rotolo desribes an electrophysiology

electrode positioning wearable sling device having a pluarlity of electrocardiographic recording electrodes positioned in contact with predetermined bust areas. Applicant maintains that the sling device provides no direction for assessing cardiac electrophysiolgy profile of a Kv1.5 antagonist.

This is not found to be persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, the combined teachings of Pugsley and Gehrmann teach the claimed recording/stimulating catheter placement for measuring arterial refractoriness and conduction in sodium and potassium ion channel blocking compounds in animal model, as well as generally teaching measurement of ECG parameters. The Rotolo reference was merely included in the rejection to show that the oppositely positioned axillary and inguinal areas are known in the art to be standard areas for electrode placement when performing ECG. Absent a showing of criticality of catheter and electrode placement for measuring EP and ECG parameters, one of ordinary skill in the art could have readily chosen from selected known positions of catheter and electrode placement with a reasonable expectation of success when testing pharmacologic effects on EP and ECG parameters.

Conclusion

No claims are allowed at this time.

Although Applicant's arguments as set forth in the aforementioned Response have been fully considered, they are deemed unpersuasive. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is (571)272-9928. The examiner can normally be reached on Monday-Wednesday 9 AM-5 PM and telework Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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